Comorbidities Associated With Increased Risk of Death among Children Aged 2-59 Months with Severe Pneumonia in Western Kenya

Timon Kwach Akoo[1*], Shehu Shagari Awandu[2], Felix Oluoch[1], Lorine Kemunto[1], Antony Ochung[1] and George Ayodo[1]

[1]Department of Public and Community Health, School of Health Sciences, Jaramogi Oginga Odinga University of Science and Technology, Bondo, Kenya and [2]Department of Biomedical Sciences School of Health Sciences, Jaramogi Oginga Odinga University of Science and Technology, Bondo, Kenya.

* **Corresponding author**: Timon Kwach Akoo, Email: kwachtimmy@yahoo.com

DOI: https://dx.doi.org/10.4314/ajhs.v36i1.2

Abstract

BACKGROUND

Globally, severe pneumonia remains the leading infectious cause of death in children younger than 5 years. Comorbidities increase the risk of death among children with severe pneumonia across age groups and regions; however, the data is scanty on specific comorbidities. The study, therefore, was aimed at improving an understanding of the risk of death due to different comorbidities among children with severe pneumonia. The findings will not only inform the clinical practices but also improve the interventions.

METHODOLOGY

We conducted a hospital-based cross-sectional study of 141 children aged 2-59 months in Bondo Sub-County hospital in Western Kenya using inpatient data health records of children admitted to the pediatric ward. Both descriptive and inferential statistics were used to determine the occurrence of comorbidities and the risk of death due to comorbidities.

RESULTS

The findings show that 57.5% of the children had at least one type of comorbidity including 36.5% malnutrition, 28.6% HIV exposed uninfected, 25.4% sickle cell disease, 7.9% HIV infected and 1.6% other comorbidities. Our findings showed that a child admitted to the hospital with comorbidities had six times increased risk of death compared to a child with severe pneumonia only [OR 6.06 (1.32-27.78) P = 0.02]. We also observed four times increased risk of death among HIV-exposed uninfected children [OR 3.92 95% CI (1.18-13.04) P = 0.03] and the risk of death increased six times when children had both HIV-exposed uninfected and malnutrition as comorbidities [OR 6.02 95% CI (1.61-22.58) P = 0.008]

CONCLUSION

High comorbidities among children with severe pneumonia and increased risk of death, in HIV-exposed uninfected and malnourished children. There is a need for improved clinical practice and intervention for severe pneumonia, HIV exposed uninfected children. There should be a review of the immunization schedule for pneumonia among HIV-exposed uninfected children.

Keywords: *Comorbidities, Severe Pneumonia, HIV Exposure Uninfected, Malnutrition*

[***Afr. J.*** *Health Sci*. 2023 36 (1): 2-9]

Introduction

Severe pneumonia is a leading cause of child hospitalizations and deaths globally (1). Childhood pneumonia kills an estimated 880,000 children globally each year, accounting for 16% of all childhood mortality (2). Half of the world's deaths due to pneumonia in children under the age of five years occur in Africa (3). Kenya is currently ranked among the 15 countries in Africa with the highest estimated number of deaths due to childhood severe pneumonia, with a mortality rate of 50.3 per 10,000 children under the age of 5 per year (4). However, several comorbidities such as HIV infection, HIV exposed uninfected (HIV-EU), and malnutrition reportedly influence the outcome of severe pneumonia in children under five years of age (5), While another study implicated sickle cell disease (6).

Several studies on severe pneumonia have associated comorbidities with the outcomes such as death or treatment failure; in particular, a study in South Africa showed that both HIV exposure and malnutrition were associated with an increased incidence of pneumonia (2). Among children with pneumonia in Botswana, HIV-exposed uninfected children were significantly more likely to fail treatment at 48 hours, required more days of continuous positive airway pressure or mechanical ventilation, and had higher in-hospital mortality than HIV-unexposed children (7). The study further observed that the differences in outcomes by HIV exposure status were only among children <6 months of age and were not attenuated by receipt of second-line antimicrobial therapy (7). In addition, severe acute malnutrition independently predicted death in HIV-exposed Malawian children with severe pneumonia (OR 5.1), more so than HIV-infected children (OR 2.2) (8).

A Gambian study of 190 children hospitalized with severe pneumonia found nutritional status to be more predictive than the degree of hypoxemia of survival (9). A study from Malawi analyzing over 100,000 episodes of pneumonia over 11 years found that those with severe undernutrition and with severe acute malnutrition had a 12% and 35% increase, respectively, in the odds of severe pneumonia mortality (2). In a cohort study of 4,184 Kenyan children <5 years admitted with severe pneumonia, 25% had severe acute malnutrition, and this was strongly associated with 1-year post-discharge mortality (10). Comorbidities contribute decisively to the risk of dying from severe pneumonia, However, the occurrence of these comorbidities across age groups and regions is poorly understood to inform the clinical practice and interventions (5). Therefore, there's a need to understand how comorbidities increase the risk of death among children suffering from severe pneumonia. This study's objective was to investigate the occurrence of comorbidities and determine the risk of death among children under 5 years with severe pneumonia.

Methodology

Study site

This study was conducted in Bondo sub-county hospital, Siaya County in Western Kenya, a referral health facility serving two sub-counties of Bondo and Rarieda. The region has the highest under-five mortality rate (33 deaths per 1,000 live births) in western Kenya (11). The records at the Bondo sub-county hospital shows that it has a catchment area of 33,780 with the majority (~99%) of people from the Luo ethnic group.

Study design

We used a cross-sectional study design and secondary data was collected from the inpatient data records of children admitted to the pediatric ward between July 2017 and June 2019.

Study participants

According to the hospital records, for the period of two years between July 2017 and July 2019, 182 children were admitted with severe pneumonia in the pediatric ward.

Inclusion and exclusion criteria

The study files from which secondary data was collected had all of this information;

presence/ absence of comorbidities, mid-upper arm circumference (MUAC), weight and diagnosis of severe pneumonia as per integrated management of childhood illnesses (IMCI) Guidelines. We excluded files that had missing information.

Case definitions and measurements

We classified nutritional status as severe malnutrition when a child had weight height/ length Z score (WHZ score) of <-3 sd or MUAC of < 11.5cm), moderate malnutrition (WHZ score of -2 to -3 sd or MUAC of 11.5cm – 12.4cm). In addition, the case definition for severe pneumonia was based on IMCI classification which included any danger signs, history of cough and increased breathing rate. The HIV-exposed children were children aged less than 18 months whose mothers were HIV positive, on highly active antiretroviral therapy (HAART) and were on follow-up in HIV comprehensive care clinic. HIV-positive children were those whose HIV status was confirmed by either DNA/PCR if less than 18 months or an HIV antibody test for those 18 months and above.

Sickle cell disease was confirmed in children using haemoglobin electrophoresis (Hb-electrophoresis). Some were newly diagnosed while others were follow-up-outpatients.

Sampling

The in-patient records of the children who had been admitted to the pediatric ward during the period were retrieved from the hospital archives and screened for the accuracy of the required information. Only 141 were able to meet the set criteria as shown in Figure 1.

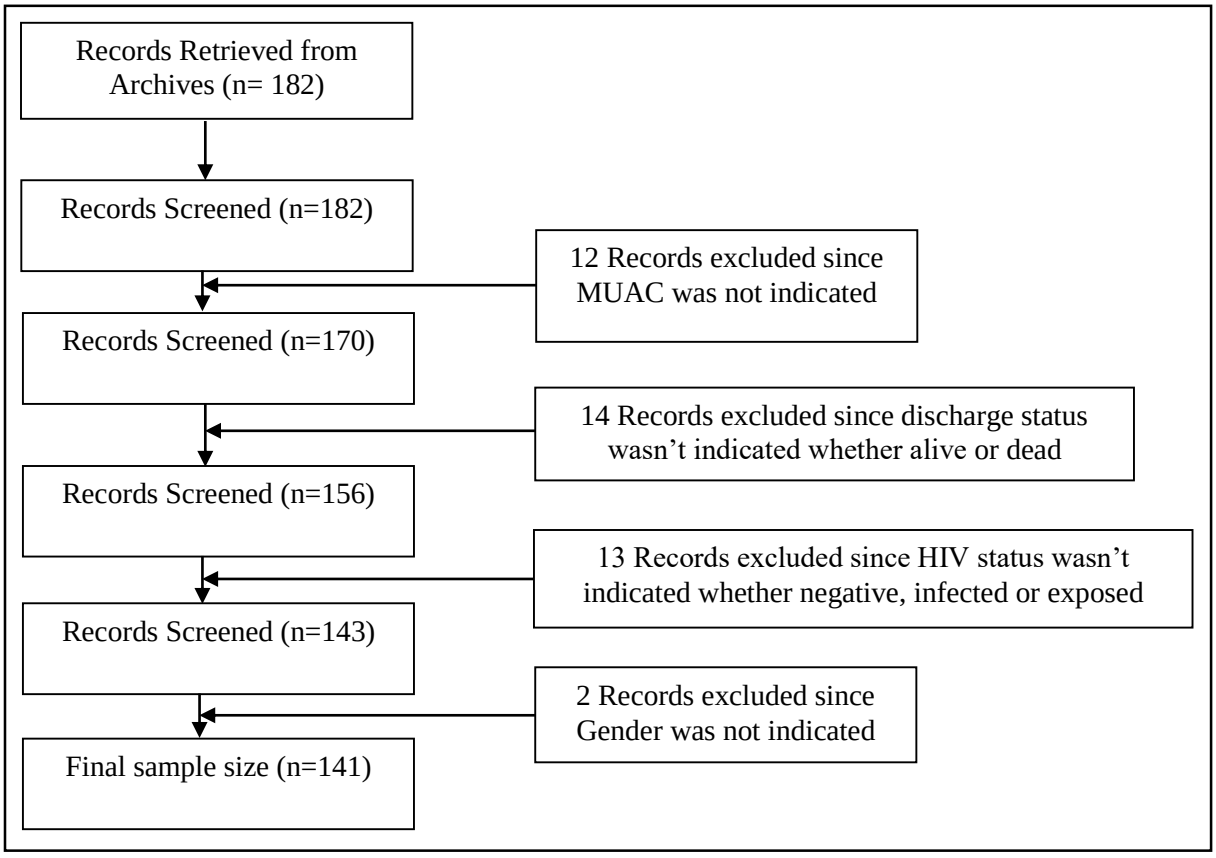

Figure 1:
Archival and screening process of in-patient records of the children who had been admitted to the pediatric ward

Reliability and validity

To enhance interpretive reliability, the contextual completeness of the data collected as well as awareness of the researcher's influence were observed consistently throughout the study. The data collection tool was pretested at a different hospital in the same area of the study.

Data analysis

Entry and analysis of data were done using SPSS version 24 (12) after which data exploration and cleaning to check the coding errors, inconsistencies, missing information and outliers were done and corrections were made appropriately. A descriptive analysis of baseline demographic characteristics was conducted. Binary logistic regression was run to assess the associations between the independent and the dependent variables and was further used to determine the risk of death due to comorbidities.

Ethical approval

Authority to carry out the research was sought from the Jaramogi Oginga Odinga Teaching and Referral Hospital Ethics and Review Committee. Approval number IERC/JOOTRH/363/20.

Results

Characteristics of study participants

The study targeted 182 patients admitted with severe pneumonia but only 141 patients met the inclusion criteria. Some of the files of the patients that had incomplete information were dropped out of the study. The mean age of the 141 patients was 16.4 months with an SD of 13.8. The majority were children below 12 months and males were 54.6% as shown in **Table 1.**

Table 1:
Children's Demographic Characteristics and the Outcome

Variable	Attribute	Frequency	Percentage %
Age in months	<12 months	70	49.6
	12-23 months	33	23.4
	24 -36 months	20	14.2
	36- 59 months	18	12.8
Gender	Male	77	54.6
	Female	64	45.4

Table 2:
The Mortality Rate of Enrolled Participants

	Patients	**Deaths**	**Mortality rate**
	n	N	%
Overall	141	16	11.4
Age in months			
<12	70	13	18.6
12-23	33	3	9.1
24 -36	20	0	0.0
36- 59	18	0	0.0
Gender			
Male	77	7	9.1
Female	64	9	14.1

The mortality rate

The overall mortality rate from severe pneumonia in this study population was 11.4%. In particular, that of children below 12 months was 18.6%, between 12 months to 23 months was 9.1% and the mortality rate of those children older than 2 years was 0.00%. Concerning gender, the mortality rate for female participants is higher than that for males (14.1% vs 9.1%).

The mortality rate

The overall mortality rate from severe pneumonia in this study population was 11.4%. In particular, that of children below 12 months was 18.6%, between 12 months to 23 months was 9.1% and the mortality rate of those children older than 2 years was 0.00%. Concerning gender, the mortality rate for female participants is higher than that for males (14.1% vs 9.1%).

The distribution of comorbidities

Data shows that 44.6% (63 out of 141) of the children had severe pneumonia and other conditions (comorbidities). The distribution of comorbidities was as follows; 7.9% were HIV infected, 28.6% were HIV exposed, 25.4% had sickle cell disease, 36.5% had malnutrition and 1.6% had other infections as shown in **Figure 2.**

The outcome of severe pneumonia with comorbidities

Using bivariate logistic regression, we show that patients with comorbidities were 6.06 times more likely to die from severe pneumonia as compared to those with no comorbidities (OR=6.06, 95%CI=1.32,27.78, P=0.02).

We further determined the association between the specific comorbidity and the outcome as shown in **Table 3**. We observed that patients with severe pneumonia and who are HIV exposed uninfected are 3.92 times more likely to die as compared to those who were not exposed uninfected (OR=3.92, 95%CI=1.18, 13.04, P-value=0.026). However, when we adjusted for malnutrition, the odds ratio increased to 6.02 with a p-value of 0.008. This demonstrated that comorbidities affect the outcome.

.

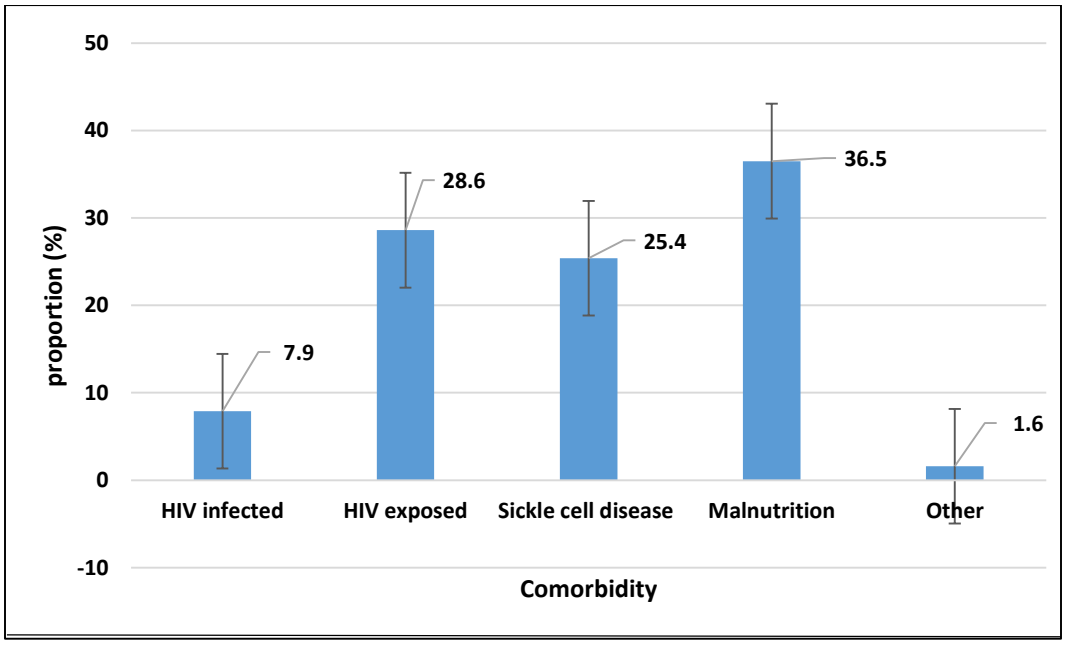

Figure 2:
The Proportion of Comorbidities among Severe Pneumonia Patients

Discussion

This study reports that children with comorbidities have an increased risk of mortality since they increase that risk of death sixfold while HIV exposed and uninfected as a comorbidity increases the risk by four folds. The overall death rate from severe pneumonia was 11.4%. In particular, that of children below 12 months was 18.6%, between 12 months to 23 months was 9.1% and the mortality rate of those children older than 2 years was 0.00%. Concerning gender, the mortality rate for female participants is higher than that for males (14.1% vs 9.1%).

These study findings are in agreement with a meta-analysis conducted among children to ascertain the risk of death from diarrhoea and pneumonia among HIV uninfected infants that showed that this group of children had a 60% chance of dying from pneumonia (5). In addition, another study showed that severe acute malnutrition independently predicted death in HIV-exposed Malawian children with pneumonia (OR 5.1), more so than HIV-infected children (OR 2.2) (8). Similarly, In a South African child health study where none of the children was HIV-infected, HIV exposure was the strongest independent risk factor for severe pneumonia (incidence rate ratio 4.04), and both HIV exposure and malnutrition were associated with an increased incidence of pneumonia (2). We have also reported the association of malnutrition with death among children suffering from severe pneumonia and indeed, malnutrition has previously been demonstrated as a predisposing factor for severe pneumonia, in particular, a Gambian study of 190 children hospitalized with hypoxemic pneumonia found nutritional status to be more predictive than the degree of hypoxemia of survival (9).

Table 2:
The Outcome of Severe Pneumonia with the Comorbidities

	Discharged n(%)	**Dead n(%)**	**OR**	**95%CI**	**P-value**
Comorbidity					
No	58(96.67)	2(3.33)	Ref		
Yes	67(82.72)	14(17.28)	6.06	1.32,27.78	0.020

Table 3:
The Outcome of Severe Pneumonia with the Specific Comorbidities

	Outcome				
	Discharged n(%)	**Dead n(%)**	**OR**	**95%CI**	**P-value**
HIV Infected					
No	121(88.97)	15(11.03)	Ref		
Yes	4(80.00)	1(20.00)	2.01	0.21, 19.25	0.542
HIV exposed					
No	112(91.06)	11(8.94)	Ref		
Yes	13(72.22)	5(27.78)	3.92	1.18, 13.04	0.026
Sickle cell anaemia					
No	111(88.80)	14(11.20)	Ref		
Yes	14(87.50)	2(12.50)	1.13	0.23, 5.51	0.877
Malnutrition					
No	107(90.68)	11(9.32)	Ref		
Yes	18(78.26)	5(21.74)	2.70	0.84, 8.70	0.096

This is further supported by a study from Malawi analyzing over 100,000 episodes of pneumonia over 11 years found that those with severe undernutrition and with severe acute malnutrition had a 12% and 35% increase, respectively, in the odds of pneumonia mortality (2). Similarly, in a cohort study of 4,184 Kenyan children <5 years admitted with severe pneumonia, 25% had severe acute malnutrition, and this was strongly associated with 1-year post-discharge mortality (10).

Using routine data from a health facility in western Kenya, we have replicated the previous research findings that comorbidities increase the risk of death among children with severe pneumonia. This demonstrates that routine data is useful not only for monitoring the quality of care (15) but also if well utilized can be useful for highlighting areas of concern for action and strategies (16). In this regard, our study shows that comorbidities increase the risk of death, and further action should be taken to address the concerns. Of significance in our findings is the need to exploit the routine data to support the continuity of clinical care or assess the standards or quality of data.

We observed that malnutrition increases the risk of death of HIV-exposed uninfected children up to six times, consequently, there is a need to come up with measures to reduce death among these groups. There is a need to explore aggressive management with the correct dosing of the recommended first-line antibiotics as well as close monitoring for antibiotic treatment failure to adjust the treatment to the second line without any unnecessary delays to reduce mortality. It is important to determine if exposure to HIV -1 and /or ART in utero or during infancy has direct immunological consequences that increase the vulnerability of this population (13, 14). Consequently, there is a need for improved clinical practice and intervention for severe pneumonia among these children but specifically, HIV-exposed uninfected children. We recommend a review of the immunization schedule for pneumonia among HIV-exposed uninfected children

As much as our study demonstrates the potential of the routine data and risk of death among severe pneumonia, our study is limited by the relatively small sample size due to poor record keeping for instance, incomplete or missing data. Also, we could not associate other comorbidities with the risk of death due to a low number of cases. Finally, due to inadequate records, we could not control for potential confounders such as vaccination and treatment failures in this study.

The study recommends a rigorous cohort study with a larger sample size to identify additional comorbidities associated with the outcome of severe pneumonia.

References

1. **McAllister DA, Liu L, Shi T, Chu Y, Reed C, Burrows J, *et al*.** Global, regional, and national estimates of pneumonia morbidity and mortality in children younger than 5 years between 2000 and 2015: a systematic analysis. *The Lancet Global Health*. 2019;7(1):e47-e57.
2. **Le Roux DM, Myer L, Nicol MP, Zar HJ.** Incidence and severity of childhood pneumonia in the first year of life in a South African birth cohort: the Drakenstein Child Health Study. *The Lancet Global Health.* 2015;3(2):e95-e103.
3. **Mathers BM, Degenhardt L, Phillips B, Wiessing L, Hickman M, Strathdee SA, *et al*.** Global epidemiology of injecting drug use and HIV among people who inject drugs: a systematic review. *The Lancet.* 2008;372(9651):1733-45.
4. **Hespanhol V, Bárbara C**. Pneumonia mortality, comorbidities matter? Pulmonology. 2020;26(3):123-9.
5. **Brennan AT, Bonawitz R, Gill CJ, Thea DM, Kleinman M, Long L, *et al*.** A meta-analysis assessing diarrhoea and pneumonia in HIV-exposed uninfected compared with HIV-unexposed uninfected infants and

children. *Journal of acquired immune deficiency syndromes* (1999). 2019;82(1):1.
6. **Miller ML, Gao G, Pestina T, Persons D, Tuomanen E.** Hypersusceptibility to invasive pneumococcal infection in experimental sickle cell disease involves platelet-activating factor receptor. *The Journal of infectious diseases.* 2007;195(4):581-4.
7. **Kelly MS, Wirth KE, Steenhoff AP, Cunningham CK, Arscott-Mills T, Boiditswe SC, *et al*.** Treatment failures and excess mortality among HIV-exposed, uninfected children with pneumonia. *Journal of the Pediatric Infectious Diseases Society.* 2015;4(4):e117-e26.
8. **Preidis GA, McCollum ED, Mwansambo C, Kazembe PN, Schutze GE, Kline MW.** Pneumonia and malnutrition are highly predictive of mortality among African children hospitalized with human immunodeficiency virus infection or exposure in the era of antiretroviral therapy. *The Journal of Paediatrics*. 2011;159(3):484-9.
9. **West T, Goetghebuer T, Milligan P, Mulholland EK, Weber M.** Long-term morbidity and mortality following hypoxaemic lower respiratory tract infection in Gambian children. *Bulletin of the World Health Organization.* 1999;77(2):144.
10. **Ngari MM, Fegan G, Mwangome MK, Ngama MJ, Mturi N, Scott JAG, *et al*.** Mortality after inpatient treatment for severe pneumonia in children: a cohort study. *Paediatric and perinatal epidemiology*. 2017;31(3):233-42.
11. **Mulatya DM, Mutuku FW.** Assessing comorbidity of diarrhoea and acute respiratory infections in children under 5 years: evidence from Kenya's demographic health survey 2014. *Journal of primary care & community health.* 2020;11:2150132720925190.
12. An overview of IBM® SPSS® statistics. (2018). IBM SPSS Statistics 25 Step by Step, 15-21. https://doi.org/10.4324/9781351033909-7
13. **Afran L, Garcia Knight M, Nduati E, Urban B, Heyderman RS, Rowland-Jones SL**. HIV-exposed uninfected children: a growing population with a vulnerable immune system? *Clinical & Experimental Immunology.* 2014;176(1):11-22.
14. **Evans C, Jones CE, Prendergast AJ.** HIV-exposed, uninfected infants: new global challenges in the era of paediatric HIV elimination. *The Lancet infectious diseases.* 2016;16(6):e92-e107.
15. **Harries AD, Zachariah R, Maher D**. The power of data: Using routinely collected data to improve public health programmes and patient outcomes in low-and middle-income countries. *Wiley Online* Library; 2013. p. 1154-6.
16. **Omore, R., Tate, J. E., O'Reilly, C. E., Ayers, T., Williamson, J., Moke, F., Schilling, K. A., Awuor, A. O., Jaron, P., Ochieng, J. B., Oundo, J., Parashar, U. D., Parsons, M. B., Bopp, C. C., Nasrin, D., Farag, T. H., Kotli8off, K. L., Nataro, J. P., Panchalingam, S., … Breiman, R. F.** (2016). Epidemiology, seasonality and factors associated with rotavirus infection among children with moderate-to-Severe diarrhoea in rural western Kenya, 2008–2012: *The global enteric multicenter study* (GEMS). *PLOS ONE*, *11*(8), e0160060. https://doi.org/10.1371/journal.pone.0160060